

RemarksRestriction Requirement

Applicants note that the restriction requirement is made final. Applicants affirm the election of Group III. Applicants request amendment of the claims to embrace compounds wherein T may be C=O as shown by numerous examples. Applicants are hopeful that the Examiner intended to include such compounds, as there is no other group designed to embrace this linker, and Applicants note that the Examiner did not object to the inclusion of such compounds in amended claim 29. Applicants respectfully request consideration of this amendment to the “T” linking group, to also include the C=O linker.

Applicants appreciate that the Examiner has examined both bonding patterns of the pyridinyl group and phenyl/naphthyl groups.

Specification Objections

Applicants respectfully request amendment of the title to more clearly reflect the elected invention. Applicants believe that entry of the amendment to the title of the specification will address the Examiner’s objection.

35 USC 112

Applicants request amendment of Claims 1 and 2 to correct an obvious error relating to the phrase “substituted carbon bearing A2 and R3”. Applicants maintain that replacing the word “and” with the word “or” corrects the obvious error in the original claims. The A2 group is shown as a floating attachment on the E1-E5 containing ring, while R3 is likewise illustrated as a floating substituent. As a floating substituent, A2 and R3, respectively, may be attached at any available carbon (E1-E5) on the ring. The phrase “substituted carbon” clearly refers to the point of attachment (E substituent) for A2 and, respectively, R3 as further supported by the numerous examples and dependent claims. Applicants respectfully submit that the skilled artisan would recognize that the inclusion of the word “and” is an obvious error in light of the numerous examples, in which all of the examples having an R3 non-hydrogen substituent have R3 and A2 attached to different carbon atoms on the ring. The claim is clear through the structures illustrated in Claims 1 and 2 that A2 and R3 are bound to the ring containing E1-E5. Finally, Applicants cite the original specification for further support for the correction, wherein all of the examples having a non-hydrogen R3 and A2 show the point of attachment to be on different carbon atoms. Correction of the obvious error is supported by the examples, the dependent claims and further is most logical to preserve proper valence of ring. Applicants respectfully submit that this amendment to claims 1 and 2 corrects an obvious error, and may thus be entered without adding any new matter to the application. Applicants respectfully request entry of this amendment, and reconsideration

of this rejection under 35 USC 112.

**35 USC 112**  
**Enablement**

Applicants note the Examiner's statement that the specification is enabling for R3 being hydrogen and alkyl; and for R7 to be hydrogen, halo, haloalkyl, alkyl, and alkoxy.

Applicants request amendment of the claims to narrow the variables for R3 and R7; however, Applicants respectfully request reconsideration of the rejection when R3 is halo and R7 is trifluoromethoxy. Applicants note the Examiner's submission that chemical reactivity is generally considered an unpredictable factor and that no substituted compounds of general formula I of any kind have been made or used.

Applicants respectfully submit that there is ample support for R3 to additionally be halo. Applicants note that the Examples 164, 167 and 248, for example include both starting materials and teachings to enable the artisan to prepare a halo substituted molecule. Additionally, Applicants cite dependent Claim 11 in combination with the general teaching and examples having halo substituents, for support of the amendment.

Likewise, Applicants respectfully submit that there is support and enablement for R7 to also be trifluoromethoxy. Applicants point to Examples 238 through 241 as well as Example 350 and numerous other examples wherein R7 is trifluoromethoxy. Applicants maintain that the general teachings in the specification, combined with the Examples, and dependent claim 11 all provide guidance and support for the inclusion of trifluoromethoxy.

In light of the Examples having said substitutions, Applicants maintain that there are teachings to describe the reagents, starting materials, and guidance to enable the artisan to prepare such compounds of Formula I. Further, applicants point to the teachings in the Examples that provide guidance to enable the artisan to obtain appropriate starting materials to use the general methods described by the specification. Applicants respectfully request reconsideration and withdrawal of this rejection under 35 USC 112.

**35 USC 112**  
**Enablement for hydrates and solvates**

Applicants request amendment of the claims to limit the claims to the compounds of Formula I or salts thereof. Applicants request deletion of the phrase "solvate, hydrate, or stereoisomer". Applicants point to both the examples and page 90 wherein the compounds of the invention or their salts are referred to. Applicants

respectfully request entry of the amendments to limit the claims to compound of Formula I or salts thereof. Applicants maintain that entry of these amendments will introduce no new matter and may properly be entered. Applicants believe that the amendment obviates this rejection under 35 USC 112. Favorable reconsideration and withdrawal of this rejection is courteously requested.

### **35 USC 103**

Applicants note the Examiners' rejections under 35 USC 103 (a) in light of US 4,795,753. Applicants note that the present invention differ from 4,795,753 at the variables R4, R5, Z, and additionally, the linking group at position A1 appears to be a 3-carbon alkyl that does not appear in the presently claimed invention. As the Examiner has noted, in all instances there are differences between the compounds of the cited art and the presently claimed molecules. As the Examiner properly pointed out in the rejection under 35 USC 112, the chemical arts are unpredictable. The unpredictability is further compounded when the new compound to be prepared is not identified or even taught in the art. In this instance, the prior art not only lacks teachings to prepare the desired compounds, it further lacks teachings to guide the artisan to even attempt to prepare the compounds now claimed.

Further, the Examiner cites Takagi and Tajima for the assertion that the artisan would find some motivation to extend the subunit between the Q and the phenyl, and select the necessary variables from disclosures of these applications to arrive at the presently claimed compounds. Applicants respectfully traverse the assertion and submit that the disclosures provide no suggestion that Compound 25 from Tajima and Compound 47 from Takagi are considered superior and should be further modified to prepare the compounds now claimed.

Likewise, for Morishita and Brooks, the disclosures of these applications lack guidance to select the one Example compound, 271 and further select the necessary variables and make additional changes to the disclosed compounds to prepare the compounds now claimed. It remains necessary to show ““some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness,”” but such reasoning “need not seek out precise teachings directed to the specific subject matter of the challenged claim.” *In re Kahn*, 441 F.3d 977, 988 (Fed. Cir. 2006). Applicants submit that the teachings in the cited application in no way guide the artisan to prepare the compounds claimed herein. Applicants respectfully draw the Examiner's attention to the recent decision by the U.S. Court of Appeals for the Federal Circuit in *Takeda Chemical v. Alphapharm*, 492 F.3d 1350, 83 U.S.P.Q.2D 1169 (C.A.F.C. 2007). The court began by noting that:

[i]n addition to structural similarity between compounds, a prima facie case of obviousness also requires a showing of “adequate support in the prior art” for the change in structure. ( Takaeda, 492 F.3d 1350 at 1356, quoting *In re Grabiak*, 769 F.2d 729, 731-32 (Fed. Cir. 1985).

Applicants further note that the C.A.F.C. opinion in Takeda was issued after the decision by the Supreme Court in KSR International Co. v. Teleflex Inc., 127 S.Ct. 1727 (2007). The Takeda C.A.F.C. specifically noted:

The test for prima facie obviousness for chemical compounds is consistent with the legal principles enunciated in KSR. [...] Thus, in cases involving new chemical compounds, it remains necessary to identify some reason that would have led a chemist to modify a known compound in a particular manner to establish prima facie obviousness of a new claimed compound. (492 F.3d 1350 at 1356 and 1357.)

Applicants submit that nothing in any of the cited patents directs one of ordinary skill to select the one compound 47 from Takagi and compound 25 of Tajima for further modification that would result in the compounds of Claim 1. Likewise, the artisan is not directed to select the one compound, 271 from Brooks or any of the other specific compounds and disclosures combined from the many cited references to arrive at the presently claimed compounds having the desired activity. It does not appear that the cited compounds were highlighted as being identified in any way as being superior to or even comparable to any other disclosed compound. Thus, Applicants submit that there is no reason for choosing the specific examples from the many examples of PPAR modulators or any other motivation that would guide one of ordinary skill to select these particular compounds for further modification. Applicants submit that the test for chemical obviousness delineated in Takeda and KSR has not been satisfied by the cited disclosures. Applicants respectfully submit that the chemical arts are unpredictable and that the cited references lack teachings to direct one of ordinary skill to choose the specific cited compounds or examples for further modification, from the many, many compounds and examples disclosed. Accordingly, reconsideration and withdrawal of the rejection are respectfully requested.

**Inventorship**

Applicants note that the joint inventors were all under a duty to assign inventions to Eli Lilly and Company at the time of any inventions claimed herein. Thus, the claimed inventions were all commonly owned at the time of any inventions covered therein. Applicants believe that there is no need for further assessment under 103(c), 102 (e), (f), or (g) prior art under 35 USC 103 (a).

**Remarks**

Applicants respectfully request entry of the enclosed amendments and reconsideration in light of both the amendments and discussion submitted herewith. Applicants believe that the case is now in condition for allowance, and request favorable reconsideration.

Respectfully submitted,

/MaCharri Vorndran-Jones/

MaCharri Vorndran-Jones  
Attorney for Applicants  
Registration No. 36,711  
Phone: 317-276-1665

Eli Lilly and Company  
Patent Division  
P.O. Box 6288  
Indianapolis, Indiana 46206-6288

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